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May 4, 2005

Director
United States patent and Trademark Office
Washington DC 20231

Attn: Dr. Larry Helms, Examiner

RE: "Antibodies as chimeric effector cell receptors against tumor antigens" #10/006,773

Dear Dr. Helms:

I am returning materials related to the USPTO action dated 2/18/2005 along with a check for the extension fee. This submission complies with the extension penalty requirement.

Thank you for your time and consideration.

Sincerely,

Richard P. Junghans, PhD, MD

Enclosure

RPJ/mj

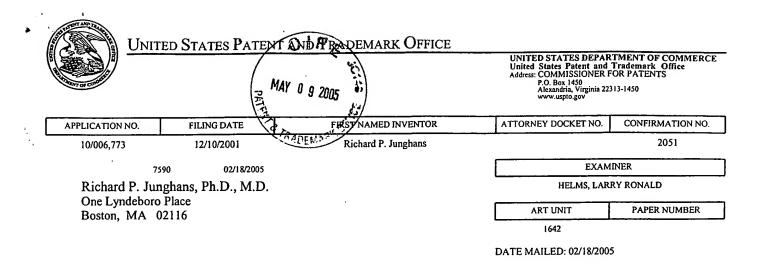
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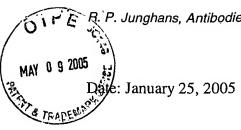
225.00 OP



1 DA	Application No.	Applicant(s)	
Notice of Non-Compliant	10/006,773	JUNGHANS, RICHARD P.	
Amendment (37 CFR 1.121) MAY 0 9 2005	Examiner	Art Unit	
	Larry R. Helms	1642	
The MAILING DAT# of this communication appears on the cover sheet with the correspondence address			
The amendment decembent filed on 25 January 2005 is corequirements of 37 CFR 1.121. In order for the amendment required.	onsidered non-compliant because ent document to be compliant, cor	e it has failed to n rection of the foll	neet the owing item(s)
THE FOLLOWING MARKED (X) ITEM(S) CAUSE THE A 1. Amendments to the specification: A. Amended paragraph(s) do not include to the specification: B. New paragraph(s) should not be under the control of the control of the specification:	markings.	E NON-COMPLI	ANT:
2. Abstract: A. Not presented on a separate sheet. 37 B. Other	CFR 1.72.		
☐ 3. Amendments to the drawings: ☐ A. The drawings are not properly identified "Annotated Sheet" as required by 37 C ☐ B. The practice of submitting proposed dra showing amended figures, without mark ☐ C. Other	FR 1.121(d). awing correction has been elimina	ited. Replaceme	nt drawings
 ✓ 4. Amendments to the claims: ☐ A. A complete listing of all of the claims is ☐ B. The listing of claims does not include th ☐ C. Each claim has not been provided with of each claim cannot be identified. Note number by using one of the following st (Previously presented), (New), (Not entermined of this amendment paper hat E. Other: claims 8 and 9 do not have the autor bracketed as required in MPEP 714. 	e text of all pending claims (includ the proper status identifier, and as e: the status of every claim must atus identifiers: (Original), (Currer ered), (Withdrawn) and (Withdraw ve not been presented in ascendi	s such, the individed the indicated after the indicated after the indicated after the indicated are indicated after the indicated after the indicated are indicated after the indicated af	dual status rits claim anceled), ided). er.
For further explanation of the amendment format required http://www.uspto.gov/web/offices/pac/dapp/opla/preognotics/		14 and the USPT	O website at
TIME PERIODS FOR FILING A REPLY TO THIS NOTICE	:		
Applicant is given no new time period if the non-comfiled after allowance. If applicant wishes to resubmit the entire corrected amendment must be resubmitted with the corrected amendment must be resubmitted.	ne non-compliant after-final amen	dment with correct	ctions, the
 Applicant is given one month, or thirty (30) days, whice corrected section of the non-compliant amendment in amendment is one of the following: a preliminary amendment for continued examination (RCE) under 37 CF period under 37 CFR 1.103(a) or (c), and an amendment of the continued examination (RCE) under 37 CFR 1.103(a) or (c). 	n compliance with 37 CFR 1.121, ndment, a non-final amendment (i R 1.114), a supplemental amendr	if the non-compli- ncluding a submi ment filed within a	ant ssion for a
Extensions of time are available under 37 CFR 1.1 amendment or an amendment filed in response to a	36(a) <u>only</u> if the non-compliant ar <i>Quayle</i> action.	mendment is a no	on-final
Failure to timely respond to this notice will result in Abandonment of the application if the non-comp filed in response to a Quayle action; or Non-entry of the amendment if the non-compliar amendment.	oliant amendment is a non-final ar		
	Y R. HELMS, PH.D MARY EXAMINER		
.S. Patent and Trademark Office	WHITE EXPONENTIAL TO THE PARTY OF THE PARTY	Part of Paper	No. 20050217



Please find below and/or attached an Office communication concerning this application or proceeding.



RESPONSE TO DETAILED ACTION

- Terms will be amended to "method" instead of "use". A clean copy of the claims are appended.
- 2. We have attached a listing of Figures modified with sequence references attached.

ELECTIONS/ RESTRICTIONS

- 3. We elect Group II, with traverse. In item #4., we argue that these are not four groups.
- 4. The four groups as outlined are related by use of a chimeric gene structure in which they are distinguished by sequence of the antibody region. Three bind to one antigen (PSMA) and one binds to another antigen (GD3). We view these as specific analogous agents from this laboratory to be covered as separate sub-claims under a single patent application.
- 5. For response, see 4.

We submit the following amended Figures to include sequence references.

Fig.3 (presently amended) shows diagram and DNA sequence of a chimeric sFv IgTCR, including the CD8α hinge modified-to-remove cysteines, within a retroviral vector. This example IgTCR molecule (using hMN14 antibody specific to CEA antigen, not part of this application) occupies nucleotides 2426 2428 to 3766 3756. (Sequences #1, 2; the vector sequences are incidental.) Equivalent versions using the antibodies MB3.6, 3D8, 4D4, 3E11 are prepared in analogous manner to create IgTCR, or other Ig-chimeric molecules.

Fig.4 (presently amended) shows the DNA sequence of:

A., B. leader plus VH (seq. #3, 4) and leader plus VL (seq. #5, 6) that specifies MB3.6.

C. As example, the VL and leader are joined with (GGSGS)3 linker to VH to create MB3.6 sFv as shown (seq. #7, nucleotides shown for amino acid seq (GGSGS)3), that is subsequently used in creating chimeric molecules. Other means of generating sFv are possible and included under this claim, as well as other means of creating antibody chimeric molecules under the intent of this invention.

D., E. leader plus VH (seq. #8, 9) and leader plus VL (seq. #10, 11) that specifies 3D8 (includes C domain sequences).

F., G. leader plus VH (seq. #12, 13) and leader plus VL (seq. #14, 15) that specifies 4D4 (includes C domain sequences).

H., I. leader plus VH (Seq. #16, 17) and leader plus VL (seq. #18, 19) that specifies 3E11 (includes C domain sequences).

These sequences are modified to prepare the sFv used in Fig.1 and Fig.3, and similarly for other constructs.

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We submit the following amended claims:

Claims

What is claimed is:

1. (previously presented) A chimeric molecule comprised of the GD3 binding domain of antibody MB3.6, with variable gene sequences as specified in Fig.4A-C, as a single chain antibody with a (GGSGS)3 linker, the zeta signaling chain of the T cell receptor and an intervening CD8α hinge in which the cysteine residues have been mutated.

2. (previously presented) A chimeric molecule comprised of the PSMA binding domain of antibody 3D8, with variable gene sequences as specified in Fig.4D&E, as a single hehain antibody with a (GGSGS)3 linker, the zeta signaling chain of the T cell receptor and an intervening CD8α hinge in which the cysteine residues have been mutated.

- 3. (previously presented) A chimeric molecule comprised of the PSMA binding domain of antibody 4D4, with variable gene sequences as specified in Fig.4F&G, as a single chain antibody with a (GGSGS)3 linker, the zeta signaling chain of the T cell receptor and an intervening CD8α hinge in which the cysteine residues have been mutated.
- 4. (previously presented): A chimeric molecule comprised of the PSMA binding domain of antibody 3E11, with variable gene sequences as specified in Fig.4H&I, as a single chain antibody with a (GGSGS)3 linker, the zeta signaling chain of the T cell receptor and an intervening CD8α hinge in which the cysteine residues have been mutated.

- 5. (previously presented) Molecules of claim 1-4 in which other signaling chains of T cells or other cell types are substituted, or in which a different hinge molecule or no hinge molecule is substituted, or a combination thereof.
- 6. (previously presented) Molecules of claim 1-5 in which at least one of the CDRs of the heavy chain and one of the CDRs of the light chain are preserved in a form (e.g., sFv or Fab) that maintains the binding of the antigen, and/or in which the linker is of different composition. For MB3.6, this specification may be met by one CDR of the heavy chain to maintain antigen binding because of the small size of the ganglioside antigen.
- 7. (previously presented) Molecules of claim 1-6 which has been modified in DNA or protein sequence but which retains the specificity and action of these molecules.
- 8. (presently amended) The use of methods of applying molecules of claims 1-7 expressed in T cells or NK cells or other effector cells to treat patients with cancers expressing the GD3 (MB3.6 derivatives) or PSMA antigen (3D8, 4D4, 3E11 derivatives).
- 9. (presently amended). The combination use of methods of applying of molecules of claims 1-7 expressed in T cells or NK cells or other effector cells to treat patients with cancers expressing the GDS (ND3.6 derivatives) or PSMA antigen (3D8, 4D4, 3E11 derivatives), together with with heterologous constructs to engage additional stimulatory and functional properties of the effector cells to enhance the antitumor therapeutic efficacy.